CLAIMS

WHAT IS CLAIMED IS:

1. A macromolecule or molecular complex for use in assaying and screening for a biological target species or environment which:

a) contains a magnetically active nucleus;

b) is capable of binding the biological target species; and

c) gives rise to a magnetic resonance signal with a unique magnetic resonance property that:

i) occurs or changes with the occurrence of said binding event between the macromolecule or molecular complex and the biological target species and/or

ii) occurs or changes with a subsequent change in the environment of the biological target species after said binding occurs.

2. The macromolecule or molecular complex according to Claim 1, wherein said binding to the biological target species is either *in vivo* or *in vitro*.

3. The macromolecule or molecular complex according to Claim 1, wherein said macromolecule or molecular complex includes a structure selected from a group consisting of monoclonal antibodies, dendrimers, self-assembled lipid complexes, liposomes, cyclodextrins, cryptands, cryptophanes, carcerands, microbubbles, micelles, vesicles, fullerenes, and molecular cage structures.

4. The macromolecule or molecular complex according to Claim 1, wherein the macromolecule or molecular complex comprises a magnetically active gas contained within a molecular carrier.

5. The macromolecule or molecular complex according to Claim 4, wherein said magnetically active gas is selected from a group consisting of hyperpolarized xenon, sulfur hexafluoride, and hyperpolarized helium.

6. The macromolecule or molecular complex according to Claim 1, wherein the

macromolecule or molecular complex contains a self-assembled lipid complex.

7. The macromolecule or molecular complex according to Claim 6, wherein said self-assembled lipid complex is a liposome.

8. The macromolecule or molecular complex according to Claim 1, wherein the macromolecule or molecular complex is a rapidly exchanging complex between a macromolecule and a magnetically active gas.

9. The macromolecule or molecular complex according to Claim 8, wherein said magnetically active gas is selected from a group consisting of hyperpolarized xenon, sulfur hexafluoride, and hyperpolarized helium.

10. The complex according to Claim 8, wherein said macromolecule is selected from a group consisting of cyclodextrins, cryptands, cryptophanes, carcerands, fullerenes, and molecular cage structures.

11. The macromolecule or molecular complex according to Claim 1, wherein said unique magnetic resonance property is selected from a group consisting of chemical shifts and relaxation times.

12. The macromolecule or molecular complex according to Claim 1, wherein said change in environment of the target species includes a change in pH, ion concentration, or concentration of other molecules near the target species.

13. A functionalized active-nucleus complex that selectively associates with a biological target species, wherein the functionalized active-nucleus complex comprises:

a) an active-nucleus and

b) a targeting carrier comprising:

i) a first binding region having at least a minimal transient binding of

said active-nucleus to form the functionalized active-nucleus complex that produces a detectable signal when the functionalized active-nucleus complex associates with the target species and

ii) a second binding region that selectively associates with the target species.

14. A functionalized active-nucleus complex according to Claim 13, wherein the functionalized active-nucleus complex is selected from a group consisting of a nuclear magnetic resonance reporter species and a magnetic resonance imaging contrast agent.

15. A functionalized active-nucleus complex according to Claim 13, wherein said active-nucleus is selected from a group consisting of hyperpolarized xenon, sulfur hexafluoride, ^{19}F derivatives, and hyperpolarized helium.

16. A functionalized active-nucleus complex according to Claim 13, wherein said targeting carrier includes a structure selected from a group consisting of monoclonal antibodies, dendrimers, self-assembled lipid complexes, liposomes, cyclodextrins, cryptands, cryptophanes, carcerands, microbubbles, micelles, vesicles, fullerenes, and molecular cage structures.

17. A functionalized active-nucleus complex according to Claim 13, wherein said second binding region and said first binding region are coextensive or essentially the same structure.

18. A functionalized active-nucleus complex according to Claim 13, wherein:

a) said active-nucleus comprises hyperpolarized xenon and

b) said first binding region comprises a cryptophane.

19. A functionalized active-nucleus complex according to Claim 18, further comprising a solubilizing region associated with said targeting carrier.

20. A functionalized active-nucleus complex according to Claim 19, wherein said solubilizing region comprises a moiety that enhances the solubility of the functionalized active-nucleus complex in a desired environment.

21. A functionalized active-nucleus complex according to Claim 19, wherein said solubilizing region comprises at least one amino acid.

22. A functionalized active-nucleus complex according to Claim 18, further comprising a tether connecting said first and second binding regions.

23. A functionalized active-nucleus complex according to Claim 19, wherein said solubilizing region comprises a moiety bound to said tether.

24. A functionalized active-nucleus complex that selectively associates with a biomolecular target species, wherein the functionalized active-nucleus complex comprises:

a) an active-nucleus and

b) a targeting carrier comprising:

i) a first binding region having at least a minimal transient binding of said active-nucleus to form the functionalized active-nucleus complex that produces a detectable signal when the functionalized active-nucleus complex associates with the target species;

ii) a second binding region that selectively associates with the target species; and

iii) a tether region connecting said first and said second binding regions.

25. A functionalized active-nucleus complex according to Claim 24, wherein the functionalized active-nucleus complex is selected from a group consisting of a

nuclear magnetic resonance reporter species and a magnetic resonance imaging contrast agent.

26. A functionalized active-nucleus complex according to Claim 24, wherein said active-nucleus is selected from a group consisting of hyperpolarized xenon, sulfur hexafluoride, polyfluorinated derivatives, and hyperpolarized helium.

27. A functionalized active-nucleus complex according to Claim 24, wherein said targeting carrier includes a structure selected from a group consisting of monoclonal antibodies, dendrimers, self-assembled lipid complexes, liposomes, cyclodextrins, cryptands, cryptophanes, carcerands, microbubbles, micelles, vesicles, fullerenes, and molecular cage structures.

28. A functionalized active-nucleus complex according to Claim 24, wherein:

a) said active-nucleus comprises hyperpolarized xenon;

b) said first binding region comprises a cryptophane; and

c) said second binding region comprises biotin.

29. A functionalized active-nucleus complex according to Claim 24, further comprising a solubilizing region associated with said tether region.

30. A functionalized active-nucleus complex according to Claim 29, wherein said solubilizing region comprises a moiety that enhances the solubility of the functionalized active-nucleus complex in a desired environment.

31. A functionalized active-nucleus complex according to Claim 29, wherein said solubilizing region comprises at least one polar group.

32. A functionalized active-nucleus complex that selectively associates with at least one biological target species, wherein the functionalized active-nucleus complex comprises:

a) an active-nucleus and

b) a targeting carrier comprising:

i) a first binding region having at least a minimal transient binding of said active-nucleus to form the functionalized active-nucleus complex that produces a detectable signal when the functionalized active-nucleus complex associates with the target species;

ii) a plurality of second binding regions, wherein each of said second binding regions selectively associates with a target species; and

iii) a plurality of tether regions wherein said first binding region is connected to each of said second binding regions by one of said plurality of said tether regions.

33. A method for assaying and screening for a biological target species which comprises:

a) functionalizing a magnetically active nucleus by incorporating said nucleus into a macromolucular or molecular complex that is capable of binding the target species;

b) bringing said macromolecular or molecular complex into contact with the target species; and

c) detecting the occurrence of or change in the nuclear magnetic resonance signal from said functionalized nucleus in order to:

i) monitor the occurrence of binding between said macromolecular or molecular complex and said target species and/or

ii) monitor a subsequent change in the environment of the target species after said binding occurs.

34. The method according to Claim 33, wherein said binding to said target species is either *in vivo* or *in vitro*.

35. The method according to Claim 33, wherein said macromolecule or molecular complex includes a structure selected from a group consisting of monoclonal antibodies, dendrimers, self-assembled lipid complexes, liposomes, cyclodextrins, cryptands, cryptophanes, carcerands, microbubbles, micelles, vesicles, fullerenes, and molecular cage structures.

36. The method according to Claim 33, wherein said macromolecular molecular complex includes a magnetically active gas contained within a molecular carrier.

37. The method according to Claim 36, wherein said magnetically active gas is selected from a group consisting of hyperpolarized xenon, sulfur hexafluoride, and hyperpolarized helium.

38. The method according to Claim 33, wherein said magnetically active gas is selected from a group consisting of hyperpolarized xenon, sulfur hexafluoride, hyperpolarized helium.

39. The method according to Claim 33, wherein said monitoring comprises detecting the occurrence of or change in a magnetic resonance signal with a unique magnetic resonance property.

40. The method according to Claim 39, wherein said magnetic resonance property is selected from a group consisting of chemical shifts and relaxation times.

41. The method according to Claim 33, wherein said change in environment of the biomolecular target comprises a change in pH, ion concentration, or concentration of other molecules near said target species.

42. A method for assaying and screening for a plurality of biological target species utilizing a plurality of functionalized active-nucleus complexes with at least two of the functionalized active-nucleus complexes having an attraction affinity to different

corresponding biological target species, comprising the steps:

a) for each functionalized active-nucleus complex, functionalizing an active-nucleus by incorporating said active-nucleus into a macromolucular or molecular complex that is capable of binding one of said target species;

b) bringing said macromolecular or molecular complexes into contact with the target species; and

c) detecting the occurrence of or change in a nuclear magnetic resonance signal from each of said active-nuclei in each of said functionalized active-nucleus complexes in order to:

i) monitor the occurrence of binding between each of said functionalized active-nucleus complexes and said target species and/or

ii) monitor a subsequent change in the environment of the target species after said binding occurs.

43. The method according to Claim 42, wherein said binding to said target species is either *in vivo* or *in vitro.*

44. The method according to Claim 42, wherein said functionalized active-nucleus complexes include structures selected from a group consisting of monoclonal antibodies, dendrimers, self-assembled lipid complexes, liposomes, cyclodextrins, cryptands, cryptophanes, carcerands, microbubbles, micelles, vesicles, fullerenes, and molecular cage structures.

45. The method according to Claim 42, wherein each said functionalized active-nucleus complex includes a magnetically active gas contained within a molecular carrier.

46. The method according to Claim 45, wherein said magnetically active gas is selected from a group consisting of hyperpolarized xenon, sulfur hexafluoride, and hyperpolarized helium.

47. The method according to Claim 42, wherein said monitoring comprises detecting the occurrence of or change in a magnetic resonance signal with a unique magnetic resonance property from each said functionalized active-nucleus complex.

48. The method according to Claim 47, wherein said magnetic resonance property is selected from a group consisting of chemical shifts and relaxation times.

49. The method according to Claim 42, wherein said change in environment of the biomolecular target comprises a change in pH, ion concentration, or concentration of other molecules near said target species.

50. A method for assaying and screening for one or more biological target species which comprises:

a) functionalizing a magnetically active nucleus by incorporating said nucleus into a macromolucular or molecular complex that is capable of binding the target species;

b) bringing said macromolecular or molecular complex into contact with the target species; and

c) detecting the occurrence of or change in the nuclear magnetic resonance signal from said functionalized nucleus in order to:

i) monitor the occurrence of binding between said macromolecular or molecular complex and said target species and/or

ii) monitor a subsequent change in the environment of the target species after said binding occurs.

51. A biosensor, comprising:

a) an environment targeting agent having an attraction affinity to a chemical environment; and

b) an active-nucleus carried by said environment targeting agent, wherein said environment targeting agent is capable of recognizing a change in said chemical environment and a detectable signal from said active-nucleus

indicates said change in said chemical environment.

52. A biosensor according to Claim 51, wherein said environment targeting agent comprises an active-nucleus binding region for carrying said active-nucleus and an environment recognition region, wherein said active-nucleus binding region is selected from a group consisting essentially of monoclonal antibodies, dendrimers, self-assembled lipid complexes, liposomes, cyclodextrins, cryptands, carcerands, microbubbles, micelles, vesicles, fullerenes, and general molecular cage structures.

53. A biosensor according to Claim 51, wherein said active-nucleus is selected from a group consisting essentially of hyperpolarized xenon, sulfur hexafluoride, and hyperpolarized helium.

54. A biosensor according to Claim 51, wherein recognition of said chemical environment by said environment targeting agent produces a detectable chemical shift from said active-nucleus.

55. A biosensor according to Claim 51, wherein recognition of said chemical environment by said environment targeting agent produces a magnetic resonance signal.

56. A biosensor according to Claim 51, wherein said change in said chemical environment is selected from a group consisting of ion channel functioning, neuron functioning, ion binding and transport, and oxygen distribution.

57. A biosensor mixture, comprising a plurality of functionalized active-nucleus complexes, at least two of the functionalized active-nucleus complexes having an attraction affinity to different corresponding target species, wherein each of said functionalized active-nucleus complexes comprises:

a) an active-nucleus and

b) a targeting carrier comprising:

i) a first binding region having at least a minimal transient binding of said active-nucleus to form the functionalized active-nucleus complex that produces a detectable signal when the functionalized active-nucleus complex associates with the target species and
ii) a second binding region that selectively associates with the target species.

58. A biosensor mixture according to Claim 57, wherein each of the functionalized active-nucleus complexes is selected from a group consisting of a nuclear magnetic resonance reporter species and a magnetic resonance imaging contrast agent.

59. A biosensor mixture according to Claim 57, wherein each of said active-nuclei is selected from a group consisting of hyperpolarized xenon, ^{19}F derivatives, sulfur hexafluoride, and hyperpolarized helium.

60. A biosensor mixture according to Claim 57, wherein each of said targeting carriers includes a structure selected from a group consisting of monoclonal antibodies, dendrimers, self-assembled lipid complexes, liposomes, cyclodextrins, cryptands, cryptophanes, carcerands, microbubbles, micelles, vesicles, fullerenes, and molecular cage structures.

61. A biosensor mixture according to Claim 57, wherein each of said second binding regions and said first binding regions are coextensive or essentially the same structure.

62. A biosensor mixture according to Claim 57, wherein:
a) said active-nucleus comprises hyperpolarized xenon and
b) said first binding region comprises a cryptophane.

63. A biosensor mixture according to Claim 57, wherein each said targeting carrier further comprises a solubilizing region associated with each said targeting carrier.

64. A biosensor mixture according to Claim 63, wherein each said solubilizing region comprises a moiety that enhances the solubility of the functionalized active-nucleus complex in a desired environment.

65. A biosensor mixture to Claim 64, wherein each said solubilizing region comprises at least one amino acid.

66. A biosensor mixture according to Claim 57, wherein each said functionalized active-nucleus complex further comprises a tether connecting said first and second binding regions.

67. A biosensor mixture according to Claim 66, wherein each said functionalized active-nucleus complex includes a solubilizing region bound to said tether.

68. A biosensor mixture, comprising:

a) a plurality of functionalized active-nucleus complexes, at least two of said functionalized active-nucleus complexes having an attraction affinity to different corresponding chemical environments and

b) an active-nucleus carried by each of said functionalized active-nucleus complexes, wherein each said active-nucleus produces a detectable signal in said chemical environment.

69. A biosensor mixture according to Claim 68, wherein each said functionalized active-nucleus complexes includes a targeting carrier that is selected from a group consisting of monoclonal antibodies, dendrimers, self-assembled lipid complexes, liposomes, cyclodextrins, cryptands, cryptophanes, carcerands, microbubbles, micelles, vesicles, fullerenes, and general molecular cage structures.

70. A biosensor mixture according to Claim 68, wherein each said active-nucleus is selected from a group consisting of hyperpolarized xenon, sulfur hexafluoride, and

hyperpolarized helium.

71. A biosensor mixture according to Claim 68, wherein said detectable signal is an NMR chemical shift.

72. A biosensor mixture according to Claim 68, wherein said detectable signal is a magnetic resonance signal.